International Journal of Research and Applied Innovations (IJRAI)

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

Bioenhancers in Herbal Medicine: Mechanisms and Therapeutic Applications

Nisha*, Subhi Sharma, MD Nasiruddin Khan, Ritik Raushan

School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab, India

***Corresponding Author: sharmanishii8@gmail.com**

ABSTRACT: Bioenhancers function as bioavailability enhancers which are pharmacologically active agents that enhance drug bioavailability and efficacy when used together with medications while remaining inactive on their own target. Herbal bioenhancers have received significant attention during the last few decades because they are naturally derived substances with low toxicity and multiple action mechanisms. The metabolic enzymes and efflux transporters and gastrointestinal absorption of drugs can be modulated by the herbal constituents such as piperine from Piper nigrum, glycyrrhizin from Glycyrrhiza glabra, and quercetin from various flavonoid-rich plants. The review describes herbal bioenhancer mechanisms while evaluating plant-derived absorption enhancers and their therapeutic applications for various drug classes. The increasing interest in polyherbal formulations and synergistic drug development creates new possibilities in clinical pharmacology and drug delivery through the study of bioenhancers in herbal medicine.

KEYWORDS: Bioenhancers, herbal medicine, piperine, bioavailability, phytochemicals, metabolism inhibitors, herbal synergy.

I. INTRODUCTION

The effectiveness of drug therapy depends on the pharmacokinetic properties of the drug including absorption distribution metabolism and excretion (ADME). The main difficulty in pharmacology exists in the low oral bioavailability of numerous drugs particularly those obtained from herbal sources and those classified under Biopharmaceutics Classification System (BCS) class II or IV [1, 2]. The solution to this problem has been investigated through research on bioenhancers which function as agents that enhance drug bioavailability when used together.

The term "bioenhancer" was popularized by Indian scientists during the 1970s at the Regional Research Laboratory (now CSIR-IIM Jammu) while studying traditional Ayurvedic formulations .Among the first such substances to be identified was piperine, the active component of black pepper (Piper nigrum), which was found to enhance the bioavailability of rifampicin and several other drugs [3].

The delivery of drugs through herbal pharmacology requires bioenhancers to boost delivery methods while using smaller medication doses and minimizing toxic effects and creating therapeutic synergy. This review evaluates the pharmacological basis and mechanisms of action and therapeutic applications of herbal bioenhancers and their significance in modern integrative medicine [4, 5].

II. MECHANISMS OF ACTION

Herbal bioenhancers produce their effects by multiple mechanisms which target various stages of drug pharmacokinetics. The mechanisms include drug-metabolizing enzyme modulation, efflux transporter inhibition, membrane permeability enhancement, and drug solubility and stability improvement (Figure 1) [6, 7].

International Journal of Research and Applied Innovations (IJRAI)

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

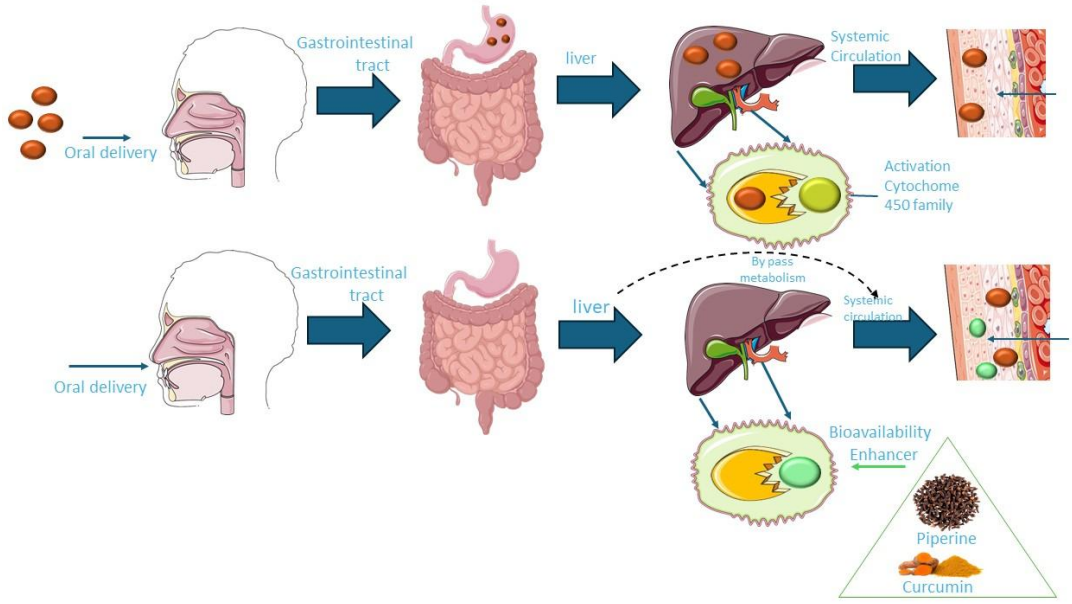

Figure 1: Mechanism of Oral Drug Absorption and Bioavailability Enhancement via Piperine and Curcumin

2.1 Inhibition of Drug-Metabolizing Enzymes (e.g., CYP450 enzymes)
The liver and intestinal tissues perform extensive first-pass metabolism on many drugs through cytochrome P450 (CYP) enzymes. Herbal bioenhancers can inhibit these enzymes, reducing the metabolic degradation of drugs and thus increasing their plasma concentration and duration of action.

Piperine, one of the most studied herbal bioenhancers, significantly inhibits the activity of CYP3A4 and CYP2D6 enzymes, both of which are involved in the metabolism of a wide range of pharmaceuticals. The inhibition process leads to increased systemic availability of drugs including rifampicin, phenytoin and propranolol [8, 9].

2.2 Inhibition of Efflux Transporters (e.g., P-glycoprotein)
The membrane protein P-glycoprotein (P-gp) functions as an efflux pump which actively removes drugs from cells to decrease their intracellular drug levels. Several herbal compounds act as P-gp inhibitors, allowing higher intracellular drug accumulation, particularly in the intestinal epithelium and the blood-brain barrier.

The P-gp inhibitory activity of quercetin and curcumin leads to improved oral bioavailability of poorly absorbed drugs including paclitaxel and digoxin [10, 11].

2.3 Enhancement of Gastrointestinal Permeability
Bioenhancers modify tight junctions in the gastrointestinal tract by changing their structure and function which enables drugs to pass through the paracellular space more easily. The lipid membranes of cells become disrupted by saponins and terpenoids found in certain herbs which results in increased membrane fluidity and permeability.

Research indicates that Piperine enhances gastrointestinal absorption through its effects on brush border enzymes and its ability to boost blood flow to the gastrointestinal mucosa [12].

2.4 Improved Solubility and Dissolution Rate
The solubility and dissolution rate of hydrophobic drugs become more soluble because certain herbal constituents function as natural surfactants or co-solvents. Zingiber officinale gingerols and Ocimum sanctum terpenoids possess solubilizing properties which improve drug dispersion and absorption [13].

International Journal of Research and Applied Innovations (IJRAI)

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

2.5 Enzyme Induction or Suppression of Conjugating Enzymes
Bioenhancers work to stop conjugation reactions including glucuronidation which limits the effectiveness of many drugs in particular cases. The example shows that curcumin blocks UDP-glucuronosyltransferase (UGT) enzymes which decreases the metabolic breakdown of curcumin and other drugs [14].

III. COMMON HERBAL BIOENHANCERS AND THEIR SOURCES

Several bioenhancers have been identified as potent bioenhancers from medicinal plants. The compounds enhance the pharmacokinetic properties of co-administered drugs and produce synergistic therapeutic effects in different situations. Below are the most studied and widely used herbal bioenhancers:

3.1 Piperine – Piper nigrum (Black Pepper)
Piperine is the most extensively studied herbal bioenhancer.It is an alkaloid present in Piper nigrum (black pepper) and Piper longum (long pepper).Piperine increases the drug absorption of curcumin and other drugs such as rifampicin, phenytoin and propranolol. Its primary mechanism involves inhibition of CYP3A4 and P-glycoprotein, as well as enhancement of intestinal absorption [15].

3.2 Quercetin – Allium cepa, Camellia sinensis, Capsicum spp.
The flavonoid compound quercetin occurs naturally in onions and green tea and apples and various other plant species. It acts as an inhibitor of several drug-metabolizing enzymes and efflux transporters like P-gp and BCRP (Breast Cancer Resistance Protein).The pharmacokinetic profile of docetaxel, paclitaxel and tamoxifen improves when quercetin is used [16].

3.3 Curcumin – Curcuma longa (Turmeric)
The active compound in turmeric known as curcumin demonstrates both anti-inflammatory and antioxidant effects. The drug blocks glucuronidation and sulfation pathways which decreases the body's ability to clear the drug from the system. Research shows that curcumin enhances the absorption of resveratrol and epigallocatechin gallate (EGCG) and particular antibiotics [17].

3.4 Glycyrrhizin – Glycyrrhiza glabra (Licorice)
Glycyrrhizin exists as a triterpenoid saponin glycoside which scientists extract from licorice roots. The compound enhances intestinal membrane permeability while specifically inhibiting hepatic enzymes especially UDP-glucuronosyltransferases (UGTs). The combination of glycyrrhizin with corticosteroids and antivirals and hepatoprotective agents is common [18].

3.5 Gingerols – Zingiber officinale (Ginger)
Gingerols are pungent phenolic compounds found in fresh ginger.The drugs modulate gastrointestinal motility and enzymatic activity to improve drug absorption. Ginger also acts as a bioenhancer by stimulating bile secretion and increasing blood flow to the intestinal mucosa [19].

IV. PHYTOCHEMICAL CLASSES ACTING AS BIOENHANCERS

Herbal bioenhancers consist of various phytochemical classes which demonstrate unique structural characteristics and functional mechanisms. The classification system enables researchers to understand how various herbal compounds affect drug bioavailability and pharmacokinetics.

4.1 Alkaloids
Alkaloids are nitrogen-containing compounds with strong biological activity.They are known for modulating enzymatic pathways and enhancing drug transport across membranes.Piperine stands out as a significant alkaloid bioenhancer which comes from Piper nigrum and Piper longum.

Piperine functions as an inhibitor of cytochrome P450 enzymes (CYP3A4 and CYP2D6) and decreases glucuronidation while enhancing intestinal absorption through its effects on brush-border enzyme activity and cell membrane dynamics. The efflux pump P-glycoprotein has been shown to be inhibited by other alkaloids such as berberine which is found in Berberis aristata [20].

International Journal of Research and Applied Innovations (IJRAI)

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

4.2 Flavonoids

The polyphenolic compound class known as flavonoids exists in large quantities throughout fruits and vegetables and medicinal herbs. They function as strong regulators of enzymes and transporters. The flavonoid Quercetin which exists in Allium cepa, Camellia sinensis and Citrus species acts as a CYP enzyme and P-gp inhibitor to increase the intracellular drug concentration of co-administered drugs.

Naringin, a flavonoid in grapefruit, is another example that inhibits intestinal CYP3A4 and improves the bioavailability of various orally administered drugs [21].

4.3 Saponins

Saponins are amphiphilic glycosides that possess surfactant-like properties. The drug permeability increases because these agents break down cell membranes and improve the solubility of drugs that are poorly soluble. Glycyrrhizin, a saponin from Glycyrrhiza glabra, has hepatoprotective effects and enhances drug absorption by affecting membrane fluidity and inhibiting UGT enzymes [22].

The bioenhancing properties of Panax ginseng and Tribulus terrestris saponins are demonstrated by their ability to increase intestinal permeability .

4.4 Terpenoids

The five-carbon isoprene units of terpenoids also known as isoprenoids produce various pharmacological effects. Gingerols are pungent phenolics that occur naturally in Zingiber officinale and function as powerful bioenhancers. The absorption of drugs improves through three mechanisms which include enhanced gastrointestinal motility and increased blood flow and modified intestinal enzyme activity (Table 1) [23].

The monoterpene limonene found in citrus oils shows potential to enhance the absorption of co-administered lipophilic drugs.

Table 1: Phytochemical Classes and Examples

Phytochemical Class	Example Compounds	Herbal Source	Bioenhancing Mechanism
Alkaloids	Piperine	*Piper nigrum*	CYP inhibition, P-gp inhibition
Flavonoids	Quercetin, Naringin	*Onion, Citrus fruits*	Enzyme & transporter modulation
Saponins	Glycyrrhizin	*Glycyrrhiza glabra*	GI permeability enhancement
Terpenoids	Gingerols, Limonene	*Zingiber officinale*	Solubility improvement, GI motility

V. THERAPEUTIC APPLICATIONS OF HERBAL BIOENHANCERS

Herbal bioenhancers function as multiple clinical and therapeutic agents which boost drug potency while requiring lower doses and enhancing safety features. Their use spans across various therapeutic classes, enhancing outcomes in infectious diseases, cancer, neurodegenerative disorders, hepatic dysfunction, and more [24].

5.1 Antimicrobial Therapy

One of the earliest and most successful applications of herbal bioenhancers has been in tuberculosis treatment.Piperine enhances the serum levels of rifampicin and isoniazid when taken together which results in better therapeutic outcomes. The combination of these drugs reduces the hepatotoxicity associated with anti-TB drugs by allowing dose reduction without affecting the efficacy.

Glycyrrhizin works synergistically with antiviral drugs such as interferon-α and lamivudine to improve their effectiveness in treating chronic hepatitis B and C infections [25].

5.2 Cancer Chemotherapy

The majority of anticancer agents face two major challenges: they have low bioavailability and they are resistant to multiple drugs (MDR). The drug efflux pumps P-gp and MRP2 become inhibited by herbal bioenhancers quercetin, curcumin and berberine which results in drug resistance reduction and higher drug concentrations inside cells [26].

International Journal of Research and Applied Innovations (IJRAI)

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

The combination of curcumin with doxorubicin, 5-fluorouracil, and cisplatin has been shown to enhance therapeutic outcomes while decreasing systemic side effects. The combination of quercetin with paclitaxel and tamoxifen results in increased breast cancer cell death through its effects on estrogen receptors and efflux transporters [27].

5.3 CNS Disorders

Bioenhancers serve as delivery tools which enhance the penetration of CNS-active drugs across the blood–brain barrier (BBB). The lipophilic properties of piperine along with its P-gp inhibition mechanism lead to increased brain drug concentrations of phenytoin, reserpine and diazepam.

The neuroprotective and bioenhancing properties of flavonoids such as baicalein and quercetin are being studied for their potential to enhance the effects of L-DOPA and cholinesterase inhibitors in the treatment of Alzheimer's disease and Parkinson's disease [28].

5.4 Hepatoprotective Therapy

Glycyrrhizin has been used in liver therapy for a long time. It enhances the activity of hepatoprotective agents and modulates inflammatory pathways associated with liver injury.It has been widely used in chronic hepatitis, non-alcoholic fatty liver disease (NAFLD), and drug-induced liver injury (DILI) (Figure 2).

Curcumin and piperine together enhance antioxidant enzyme activity and reduce oxidative stress in hepatic tissues, demonstrating significant hepatoprotective synergy [29].

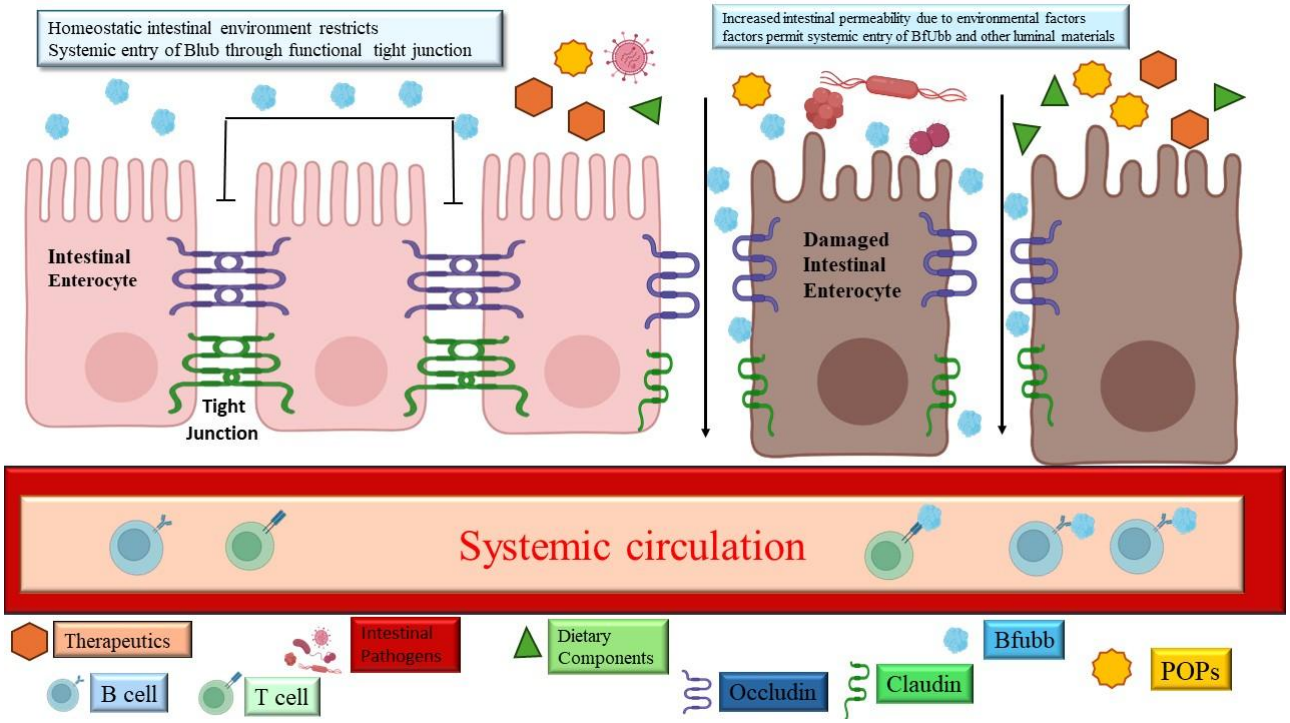

Figure 2: Mechanism of Intestinal Barrier Integrity and Systemic Entry of Luminal Components

5.5 Metabolic and Cardiovascular Disorders

The combination of gingerols and piperine enhances metformin and statin absorption which leads to improved blood sugar and lipid management. Curcumin enhances insulin sensitivity and exerts antihyperlipidemic effects when combined with piperine, which improves its systemic retention[30].

The combination of naringin and hesperidin flavonoids enhances endothelial function and strengthens the effects of antihypertensive drugs including amlodipine [11, 31].

International Journal of Research and Applied Innovations (IJRAI)

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

Table - II: Therapeutic Applications

Application Area	Key Bioenhancers	Enhanced Drugs/Effects
Antimicrobial therapy	Piperine, Glycyrrhizin	Rifampicin, Lamivudine, Interferon-α
Cancer chemotherapy	Quercetin, Curcumin	Paclitaxel, Doxorubicin, 5-FU
CNS disorders	Piperine, Baicalein	Phenytoin, Diazepam, L-DOPA
Hepatoprotective agents	Glycyrrhizin, Curcumin	Silymarin, Antivirals
Cardiometabolic therapy	Gingerols, Naringin	Metformin, Statins, Amlodipine

VI. FORMULATION STRATEGIES USING HERBAL BIOENHANCERS

The complete utilization of herbal bioenhancers requires different formulation approaches that have been developed. The goals include enhancing drug pharmacokinetics and achieving therapeutic synergy and stability while addressing issues related to poor solubility and rapid metabolism. These strategies range from traditional herbal combinations to modern nanotechnology-based delivery systems.

6.1 Conventional Herbal Combinations

Traditional medicine and Ayurveda employ Trikatu as a combination of Piper nigrum piperine and Zingiber officinale gingerols and long pepper to boost digestion and drug absorption [1]. Modern pharmacology has validated these formulations as synergistic enhancers of absorption and metabolism.

Formulations combining curcumin and piperine are now commonly marketed, as piperine increases the bioavailability of curcumin by 2000% by inhibiting its glucuronidation and increasing its intestinal absorption [32].

6.2 Nanoformulations and Drug Delivery Systems

Nanoformulation-based drug delivery systems, including nanoemulsions, solid lipid nanoparticles (SLNs), polymeric nanoparticles, and liposomes, have emerged as advanced atforms for enhancing the therapeutic potential of natural bioactive compounds. These nanocarriers are engineered to enhance stability, enable controlled and sustained release, and improve permeability across biological membranes, while also protecting sensitive phytochemicals from premature degradation. Co-delivery strategies using herbal bioenhancers offer additional advantages; for example, curcumin-loaded nanoparticles combined with piperine have demonstrated enhanced anticancer efficacy in preclinical cancer models. Similarly, quercetin-loaded nanocarriers used alongside conventional chemotherapeutics have been shown to improve intracellular drug accumulation and modulate resistance pathways, ultimately strengthening therapeutic outcomes [33, 34].

6.3 Polyherbal Synergistic Formulations

Polyherbal formulations that incorporate multiple bioenhancers are gaining increasing importance because they can influence various pharmacokinetic pathways simultaneously, resulting in enhanced multi-target therapeutic effects. For instance, the combination of curcumin, quercetin, and piperine has demonstrated strengthened anti-inflammatory and anticancer activities, while mixtures such as gingerol with glycyrrhizin exhibit complementary antiemetic and hepatoprotective properties. These synergistic interactions make such formulations particularly valuable in the management of chronic and multifactorial diseases, including cancer, arthritis, and metabolic syndrome, where single-agent therapies often show limited effectiveness [35].

6.4 Clinically Approved or Commercial Formulations

Several clinically approved or commercially available herbal-based formulations successfully incorporate bioenhancers to improve therapeutic efficacy and pharmacokinetic performance. Notable examples include Risorine**,** an anti-tuberculosis formulation consisting of rifampicin, isoniazid, and piperine, in which piperine enhances the bioavailability of rifampicin by approximately 60%, allowing dose reduction and lowering the risk of hepatotoxicity.

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

Similarly, Biocurcumax and Curcumin C3 Complex formulations utilize piperine to significantly increase the systemic absorption of curcumin, thereby enhancing its anti-inflammatory and nutraceutical benefits. Another example is Liv.52 DS, a widely used hepatoprotective polyherbal product containing botanicals such as caper bush and chicory, which possess enzyme-modulating and bioavailability-enhancing properties that support liver function [36].

6.5 Fixed-Dose Combinations and Co-Crystals

Recent advances in formulation science have focused on developing fixed-dose combinations and pharmaceutical co-crystals incorporating bioenhancers to improve therapeutic performance. These engineered systems aim to enhance solubility, enable sustained and controlled release, and ultimately increase patient compliance by reducing dosing frequency. Experimental studies demonstrate that co-crystals composed of curcumin and piperine exhibit improved physicochemical stability and more regulated release characteristics, highlighting their potential in modern drug delivery strategies [37].

VII. REGULATORY STATUS AND SAFETY CONCERNS

Despite the therapeutic potential of herbal bioenhancers, their regulatory acceptance and safety evaluation present notable challenges.The majority of these compounds originate from GRAS herbs yet their influence on drug metabolism and transport and elimination processes creates issues regarding drug–herb interactions and toxicity and dosing consistency.

7.1 Safety Evaluation of Herbal Bioenhancers

The safety evaluation of herbal bioenhancers is a critical component of their integration into modern therapeutic applications. Although compounds such as piperine, curcumin, and glycyrrhizin are generally recognized as safe when used within traditional dosing limits, their pharmacological effects can become harmful when administered at high concentrations or in combination with synthetic drugs. By altering drug absorption and plasma concentrations, bioenhancers may unintentionally increase toxicity or narrow therapeutic windows. For example, while piperine enhances rifampicin bioavailability, it also slows its clearance, which—if not carefully monitored—may elevate the risk of hepatotoxicity. Similarly, excessive intake of glycyrrhizin can lead to pseudoaldosteronism, resulting in hypertension, hypokalemia, and edema. Therefore, standardized dosing protocols, comprehensive toxicological assessment, and clinical monitoring are essential prerequisites for ensuring the safe incorporation of bioenhancers into contemporary medical practice [38].

7.2 Herb–Drug Interactions

Herbal bioenhancers exert significant influence on drug metabolism by modulating cytochrome P450 (CYP450) enzymes and efflux transporters, mechanisms that can substantially alter the pharmacokinetic profiles of co-administered drugs. While this modulation may improve therapeutic efficacy, it also carries risk for medications with a narrow therapeutic index, such as warfarin, phenytoin, cyclosporine, and digoxin, where even small changes in plasma concentration can lead to serious clinical consequences. Co-administration of these drugs with herbal bioenhancers may result in increased systemic exposure, reduced clearance, and potential toxicity. Therefore, combining herbal bioenhancers with conventional drugs must be carefully monitored under clinical supervision to ensure patient safety and avoid adverse drug interactions [39].

7.3 Regulatory Recognition

Regulatory recognition of herbal bioenhancers varies widely across global frameworks, with policies distributed across multiple independent regulatory systems.

In India, the Ministry of AYUSH actively supports the use of herbal bioenhancers, and products such as Risorine, which incorporates piperine to enhance rifampicin absorption, are approved under the Department of AYUSH and the Central Drugs Standard Control Organization (CDSCO). In contrast, the U.S. Food and Drug Administration (FDA) does not currently classify bioenhancers as a distinct drug category, although compounds such as piperine and curcumin are included on the Generally Recognized as Safe (GRAS) list and are permitted within nutraceutical and dietary supplement formulations. Within the European Union, the European Medicines Agency (EMA) regulates bioenhancers under the category of herbal medicinal products, requiring robust evidence of safety and efficacy for traditional or well-established therapeutic applications. Similarly, regulatory bodies in Japan and China integrate bioenhancers into established traditional medicine systems such as Kampo and Traditional Chinese Medicine (TCM),

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

but mandate comprehensive pharmacokinetic enhancement data and safety validation prior to approval. This heterogeneous regulatory landscape underscores the need for harmonized international guidelines to support safe and scientifically grounded clinical utilization of herbal bioenhancers [40].

VIII. FUTURE PERSPECTIVES AND RESEARCH TRENDS

Herbal bioenhancers are emerging as powerful tools for advancing modern therapeutics, with research increasingly focusing on their ability to improve drug absorption, efficacy, and safety. Future trends highlight the development of synthetic analogues with stronger potency and fewer side effects, as well as expanding applications in biologics, mRNA vaccines, and gene therapy. Computational technologies such as AI, molecular docking, and machine learning are accelerating the discovery of novel bioenhancers and predicting their pharmacokinetic behavior. Precision medicine further enables tailoring bioenhancer use to an individual's genetic makeup, enhancing treatment safety and effectiveness. To ensure wider clinical adoption, harmonized global regulations and robust randomized controlled trials are essential for validating safety, optimizing dosage, and ensuring quality. Collectively, these advancements indicate a transformative future where herbal bioenhancers play a central role in personalized, efficient, and evidence-based healthcare.

IX. CONCLUSION

Pharmacology shows promising development through herbal bioenhancers, which provide scientifically validated natural and cost-effective methods to improve drug efficacy and safety. The ability of these compounds to improve drug bioavailability through enzyme modulation and efflux transporter and membrane permeability enhancement has been established in multiple drug categories and disease states.

Compounds such as piperine, quercetin, curcumin, and glycyrrhizin have shown significant potential in clinical and preclinical settings, contributing to enhanced antimicrobial, anticancer, CNS, hepatoprotective, and metabolic therapies.Modern formulation approaches have optimized these compounds for real-world applications through the use of nano-delivery systems, polyherbal combinations and fixed-dose co-crystals.

The implementation of herbal bioenhancers faces various obstacles. The following issues require systematic resolution: standardization problems and herb-drug interactions and toxicological profiling and regulatory recognition. The increasing demand for personalized medicine and biologics and natural product-based drug development requires herbal bioenhancers to become essential for future pharmacotherapy. Further research, robust clinical trials, and regulatory harmonization will be essential to fully integrate bioenhancers into mainstream medicine, maximizing their benefits while ensuring patient safety. With careful scientific exploration and validation, bioenhancers may redefine how we approach drug delivery and therapeutic optimization in the years to come.

Conflict of Interest: None

REFERENCES

1. Ranadeep, B., et al., *Tiny Dots, Big Impact: The Antimicrobial Power of Carbon Dots.* Anti-Infective Agents, 2025. **23**(5): p. 148-157.
2. Li, Y., et al., *Current trends in drug metabolism and pharmacokinetics.* Acta Pharmaceutica Sinica B, 2019. **9**(6): p. 1113-1144.
3. Islam, M.M., et al., *Formulation Development, Box-Behnken Design-Based Optimization and Evaluation of Cisplatin-Loaded Chitosan Nanoparticles Embedded in Mucoadhesive Buccal Film for Targeted Oral Cancer Therapy.* Journal of Pharmaceutical Innovation, 2025. **20**(6): p. 276.
4. Harmanjot, K., et al., *Exosomes in Oncology: Advancing Gene Therapy and Targeted Drug Delivery Systems.* Clinical Cancer Drugs, 2025. **11**: p. 58-71.
5. Mishra, R., et al., *Flavonoids as bioenhancers: A critical review on their potential to improve drug delivery and therapeutic outcomes.* Pharmacological Research - Natural Products, 2025. **7**: p. 100251.
6. Moidul Islam, J., et al., *Therapeutic Trends in Diabetes Management: A Review on Oral Hypoglycemic Agents (OHAs) Utilization in Tertiary Care.* Cardiovascular & Hematological Disorders-Drug Targets, 2025. **25**: p. 1-17.

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

7. Gidwani, B., et al., *Herbal Bioenhancers in Pharmaceutical Drug Delivery: Mechanisms, Challenges, and Future Innovations.* Chem Biodivers, 2025. **22**(9): p. e00760.
8. Simakh, A., et al., *Battle of the Blends: Evaluating Tamsulosin-dutasteride and Silodosindutasteride in Benign Prostatic Hyperplasia Patients.* Clinical Cancer Drugs, 2025. **11**: p. 1-6.
9. Bhardwaj, R.K., et al., *Piperine, a major constituent of black pepper, inhibits human P-glycoprotein and CYP3A4.* J Pharmacol Exp Ther, 2002. **302**(2): p. 645-50.
10. Md Moidul, I., et al., *Nanotechnology in Anti-EGFR Treatments: Enhancing Delivery and Minimizing Toxicity in Cancer Therapy.* Clinical Cancer Drugs, 2025. **11**: p. 137-150.
11. Nguyen, T.T., V.A. Duong, and H.J. Maeng, *Pharmaceutical Formulations with P-Glycoprotein Inhibitory Effect as Promising Approaches for Enhancing Oral Drug Absorption and Bioavailability.* Pharmaceutics, 2021. **13**(7).
12. Md Moidul, I., et al., *Solid Lipid Nanoparticles: Preparation Methods and Therapeutic Potential in Oral Cancer.* Clinical Cancer Drugs, 2025. **11**: p. 118-132.
13. Md Moidul, I., et al., *Addressing Toxicity Concerns: State-of-the-Art Synthesis Methods and Emerging Multifaceted Applications of Silver Nanoparticles.* Current Nanomedicine, 2025. **15**(4): p. 418-431.
14. Md Moidul, I., K. Dinesh, and J. Moidul Islam, *Revolutionizing Science: Breakthroughs and Trends in Nanochemistry.* Current Engineering Letters and Reviews, 2025. **2**: p. 1-4.
15. Ashutosh, K., et al., *Modern Solutions to UTIs: The Role of Nanotechnology and Herbal Treatments.* Current Drug Targets, 2025. **26**(12): p. 828-849.
16. Sushil Kumar, S., I. Md Moidul, and P. Shyam Sunder, *Recent Approach for an Effective Treatment of Mucormycosis and Future Directions.* Anti-Infective Agents, 2026. **24**(2): p. 70-80.
17. Md Moidul, I., et al., *Targeting Cancer with Graphene Quantum Dots (GQDs): A Novel Approach.* Clinical Cancer Drugs, 2025. **11**: p. 1-11.
18. Md Moidul, I. and R. Sarjana, *Artificial Intelligence in the Development and Optimization of Nanocarriers.* Current Nanoscience, 2025. **21**(3): p. 355-357.
19. Md. Moidul, I., K. Jyotibikash, and R. Sarjana, *Upholding Data Integrity in the Pharmaceutical Industry.* Applied Drug Research, Clinical Trials and Regulatory Affairs, 2025. **11**: p. 1-4.
20. Amit, K., et al., *Liposomal Drug Delivery System for the Management of Prostate Cancer: An Update.* Current Nanomedicine, 2025. **15**: p. 1-15.
21. Md Moidul, I., V. Abhinav, and K. Manish, *Advancements Beyond Limb Loss: Exploring the Intersection of AI and BCI in Prosthetic Evaluation.* Current Pharmaceutical Design, 2024. **30**(35): p. 2749-2752.
22. Md Moidul, I., et al., *Innovative Progress: Artificial Intelligence in the Realm of Oral Cancer.* Clinical Cancer Drugs, 2024. **10**: p. 37-48.
23. Amit, K., et al., *Revolutionizing Drug Delivery: The Impact of Microsponges in Pharmaceutical Research.* Drug Delivery Letters, 2025. **15**(3): p. 205-221.
24. Abhinav, V., et al., *Navigating Drug-Drug Interactions in Multimorbid Patients: Utilizing Tools, Guidelines, and Clinical Implications.* Current Drug Safety, 2025. **20**(3): p. 247-252.
25. Md Moidul, I., V. Abhishek, and R. Sarjana, *PAMAM Dendrimers: Revolutionizing the Targeted Cancer Therapy.* Clinical Cancer Drugs, 2024. **10**: p. 12-15.
26. Tarun, S., et al., *Targeting to Overexpressed Receptor in Colon Cancer: A Review.* The International Journal of Gastroenterology and Hepatology Diseases, 2024. **3**: p. 68-75.
27. Md Moidul, I., et al., *Emerging Trends in Novel Drug Delivery Systems for the Effective Treatment of Oral Cancer.* Current Cancer Therapy Reviews, 2025. **21**(5): p. 679-694.
28. Md Moidul, I. and R. Sarjana, *Monitoring Regulatory Compliance within the Pharmaceutical Industry.* Applied Drug Research, Clinical Trials and Regulatory Affairs, 2024. **10**: p. 65-68.
29. Ashutosh, K., et al., *Transferosomes: Advancing Vesicular Drug Delivery Systems for Dermatological Disorders - A Comprehensive Review.* Current Nanomedicine, 2025. **15**(3): p. 226-240.
30. Milan Singh, K., et al., *Revolutionizing Rheumatoid Arthritis Care: AI-infused Herbal Treatments and the Road Ahead.* Current Pharmaceutical Biotechnology, 2025. **26**(3): p. 316-318.
31. Md. Moidul, I. and R. Sarjana, *Enhancement of Oral Bioavailability of Protein and Peptide by Polysaccharide-based Nanoparticles.* Protein & Peptide Letters, 2024. **31**(3): p. 209-228.
32. Kumar, A., et al., *Recent Trends in Nanocarrier-Based Drug Delivery System for Prostate Cancer.* AAPS PharmSciTech, 2024. **25**(3): p. 55.
33. Abhishek, V., et al., *Navigating the Opioid Crisis: Exploring Innovative Approaches to Pain Management.* Current Pharmaceutical Biotechnology, 2024. **25**(13): p. 1629-1631.

| ISSN: 2455-1864 | www.ijrai.org | editor@ijrai.org | A Bimonthly, Scholarly and Peer-Reviewed Journal |

||Volume 8, Issue 6, November–December 2025||

DOI:10.15662/IJRAI.2025.0806019

34. Rehman, M., et al., *Lipid-Based Nanoformulations for Drug Delivery: An Ongoing Perspective.* Pharmaceutics, 2024. **16**(11).
35. Shahzad, N., et al., *Therapeutic strategy of biological macromolecules based natural bioactive compounds of diabetes mellitus and future perspectives: A systematic review.* Heliyon, 2024. **10**(2): p. e24207.
36. Parasuraman, S., G.S. Thing, and S.A. Dhanaraj, *Polyherbal formulation: Concept of ayurveda.* Pharmacogn Rev, 2014. **8**(16): p. 73-80.
37. Kumar Bandaru, R., et al., *Recent Advances in Pharmaceutical Cocrystals: From Bench to Market.* Front Pharmacol, 2021. **12**: p. 780582.
38. Kesarwani, K., R. Gupta, and A. Mukerjee, *Bioavailability enhancers of herbal origin: an overview.* Asian Pac J Trop Biomed, 2013. **3**(4): p. 253-66.
39. Wanwimolruk, S. and V. Prachayasittikul, *Cytochrome P450 enzyme mediated herbal drug interactions (Part 1).* Excli j, 2014. **13**: p. 347-91.
40. Hegde, M., et al., *Curcumin Formulations for Better Bioavailability: What We Learned from Clinical Trials Thus Far?* ACS Omega, 2023. **8**(12): p. 10713-10746.